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RAW SEQUENCE LISTING DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:34

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Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

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      4 <110> APPLICANT: MARTHA K. NEWELL
      7 <120> TITLE OF INVENTION: METHODS AND PRODUCTS RELATED TO
      8       METABOLIC INTERACTIONS IN DISEASE
     11 <130> FILE REFERENCE: V0139/7028
C--> 13 <140> CURRENT APPLICATION NUMBER: US/09/711,022
C--> 13 <141> CURRENT FILING DATE: 2000-11-09
     13 <150> PRIOR APPLICATION NUMBER: U.S. 60/082,250
     14 <151> PRIOR FILING DATE: 1998-04-17
     16 <150> PRIOR APPLICATION NUMBER: U.S. 60/094,519
     17 <151> PRIOR FILING DATE: 1998-07-29
     19 <150> PRIOR APPLICATION NUMBER: U.S. 60/101,580
     20 <151> PRIOR FILING DATE: 1998-09-24
     22 <160> NUMBER OF SEQ ID NOS: 13
     24 <170> SOFTWARE: FastSEQ for Windows Version 3.0
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     27 <211> LENGTH: 1491
     28 <212> TYPE: DNA
     29 <213> ORGANISM: Homo Sapiens
     31 <400> SEQUENCE: 1
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     34  gtgaaactaa atccacaacc tttggagacc caggaacacc ctccaatctc tgtgtgtttt     180
     35  gtaaacatca ctggagggtc ttctacgtga gcaattggat tgtcatcagc cctgcctgtt     240
     36  ttgcacctgg gaagtgccct ggtcttactt gggtccaaat tgttggcttt cacttttgac     300
     37  cctaagcatc tgaagccatg ggccacacac ggaggcaggg aacatcacca tccaagtgtc     360
     38  catacctcaa tttctttcag ctcttggtgc tggctggtct ttctcacttc tgttcaggtg     420
     39  ttatccacgt gaccaaggaa gtgaaagaag tggcaacgct gtcctgtggt cacaatgttt     480
     40  ctgttgaaga gctggcacaa actcgcatct actggcaaaa ggagaagaaa atggtgctga     540
     41  ctatgatgtc tggggacatg aatatatggc ccgagtacaa gaaccggacc atctttgata     600
     42  tcactaataa cctctccatt gtgatcctgg ctctgcgccc atctgacgag ggcacatacg     660
     43  agtgtgttgt tctgaagtat gaaaaagacg ctttcaagcg ggaacacctg gctgaagtga     720
     44  cgttatcagt caaagctgac ttccctacac ctagtatatc tgactttgaa attccaactt     780
     45  ctaatattag aaggataatt tgctcaacct ctggaggttt tccagagcct cacctctcct     840
     46  ggttggaaaa tggagaagaa ttaaatgcca tcaacacaac agtttcccaa gatcctgaaa     900
     47  ctgagctcta tgctgttagc agcaaactgg atttcaatat gacaaccaac cacagcttca     960
     48  tgtgtctcat caagtatgga catttaagag tgaatcagac cttcaactgg aatacaacca    1020
     49  agcaagagca ttttcctgat aacctgctcc catcctgggc cattaccttа atctcagtaa    1080
     50  atggaatttt tgtgatatgc tgcctgacct actgctttgc cccaagatgc agagagagaa    1140
     51  ggaggaatga gagattgaga agggaaagtg tacgccctgt ataacagtgt ccgcagaagc    1200
     52  aaggggctga aaagatctga aggtagcctc cgtcatctct tctgggatac atggatcgtg    1260
     53  gggatcatga ggcattcttc ccttaacaaa tttaagctgt ttтacccact acctcacctt    1320
     54  cttaaaaacc tctttcagat taagctgaac agttacaaga tggctggcat ccctctcctt    1380
     55  tctccccata tgcaatttgc ttaatgtaac ctcttctttt gccatgtttc cattctgcca    1440
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            20                  25                  30
Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
        35                  40                  45
Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
    50                  55                  60
Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65                  70                  75                  80
Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
                85                  90                  95
Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
            100                 105                 110
Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
        115                 120                 125
Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr
    130                 135                 140
Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145                 150                 155                 160
Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
                165                 170                 175
Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
            180                 185                 190
Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
        195                 200                 205
Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
    210                 215                 220
Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225                 230                 235                 240
Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile Ser Val Asn Gly
                245                 250                 255
Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg
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Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val
        275                 280                 285
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<210> SEQ ID NO: 3
<211> LENGTH: 1424
<212> TYPE: DNA
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cagtggacag gcatttgtga cagcactatg ggactgagta acattctctt tgtgatggcc     180
ttcctgctct ctggtgctgc tcctctgaag attcaagctt atttcaatga gactgcagac     240
ctgccatgcc aatttgcaaa ctctcaaaac caaagcctga gtgagctagt agtatttttgg     300
caggaccagg aaaacttggt tctgaatgag gtatacttag gcaaagagaa atttgacagt     360
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Input Set : A:\V1397028.txt
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113  gttcattcca agtatatggg ccgcacaagt tttgattcgg acagttggac cctgagactt     420
114  cacaatcttc agatcaagga caagggcttg tatcaatgta tcatccatca caaaaagccc     480
115  acaggaatga ttcgcatcca ccagatgaat tctgaactgt cagtgcttgc taacttcagt     540
116  caacctgaaa tagtaccaat ttctaatata acagaaaatg tgtacataaa tttgacctgc     600
117  tcatctatac acggttaccc agaacctaag aagatgagtg ttttgctaag aaccaagaat     660
118  tcaactatcg agtatgatgg tattatgcag aaatctcaag ataatgtcac agaactgtac     720
119  gacgtttcca tcagcttgtc tgtttcattc cctgatgtta cgagcaatat gaccatcttc     780
120  tgtattctgg aaactgacaa gacgcggctt ttatcttcac ctttctctat agagcttgag     840
121  gaccctcagc ctcccccaga ccacattcct tggattacag ctgtacttcc aacagttatt     900
122  atatgtgtga tggttttctg tctaattcta tggaaatgga agaaggaaga gcggcctcgc     960
123  aactcttata aatgtggaac caacacaatg gagagggaag agagtgaaca gaccaagaaa    1020
124  agagaaaaaa tccatatacc tgaaagatct gatgaagccc agcgtgtttt taaaagttcg    1080
125  aagacatctt catgcgacaa aagtgataca tgtttttaat taaagagtaa agcccataca    1140
126  agtattcatt ttttctaccc tttcctttgt aagttcctgg gcaaccttct tgatttcttc    1200
127  cagaaggcaa aaagacatta ccatgagtaa taaggggact ccaggactcc ctctaagtgg    1260
128  aataqcctcc ctgtaactcc agctctgctc cgtatgccaa gaggagactt taattctctt    1320
129  actgcttctt ttcacttcag agcacactta tgggccaagc ccagcttaat ggctcatgac    1380
130  ctggaaataa aatttaggac caataaaaaa aaaaaaaaaa aaaa                     1424
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133 <211> LENGTH: 323
134 <212> TYPE: PRT
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141              20                  25                  30
142  Pro Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val
143          35                  40                  45
144  Val Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu
145      50                  55                  60
146  Gly Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Gly Arg Thr
147  65                  70                  75                  80
148  Ser Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile
149                  85                  90                  95
150  Lys Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr
151              100                 105                 110
152  Gly Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala
153          115                 120                 125
154  Asn Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn
155      130                 135                 140
156  Val Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro
157  145                 150                 155                 160
158  Lys Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr
159                  165                 170                 175
160  Asp Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp
161              180                 185                 190
162  Val Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met
163          195                 200                 205
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Input Set : A:\V1397028.txt
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164  Thr Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser
165      210                 215                 220
166  Pro Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile
167  225                 230                 235                 240
168  Pro Trp Ile Thr Ala Val Leu Pro Thr Val Ile Ile Cys Val Met Val
169                  245                 250                 255
170  Phe Cys Leu Ile Leu Trp Lys Trp Lys Lys Lys Lys Arg Pro Arg Asn
171              260                 265                 270
172  Ser Tyr Lys Cys Gly Thr Asn Thr Met Glu Arg Glu Glu Ser Glu Gln
173          275                 280                 285
174  Thr Lys Lys Arg Glu Lys Ile His Ile Pro Glu Arg Ser Asp Glu Ala
175      290                 295                 300
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189  ctccaggtcc aaggtgaatg cccgacgtcc agtgttatta ggtataaagg tgtcctggga     180
190  acaatcaccg ctgtggtaaa aacagaaggg cggatgaaac tctacagcgg gctgcctgcg     240
191  gggcttcagc ggcaaatcag ctccgcctct ctcaggatcg gcctctacga cacggtccag     300
192  gagttcctca ccgcagggaa agaaacagca cctagtttag gaagcaagat tttagctggt     360
193  ctaacgactg gaggagtggc agtattcatt gggcaaccca cagaggtcgt gaaagtcaga     420
194  cttcaagcac agagccatct ccacggaatc aaacctcgct acacggggac ttataatgcg     480
195  tacagaataa tagcaacaac cgaaggcttg acgggtcttt ggaaagggac tactcccaat     540
196  ctgatgagaa gtgtcatcat caattgtaca gagctagtaa catatgatct aatgaaggag     600
197  gcctttgtga aaaacaacat attagcagat gacgtccccc gccacttggt gtcggctctt     660
198  atcgctggat tttgcgcaac agctatgtcc tccccggtgg atgtagtaaa aaccagattt     720
199  attaattctc caccaggaca gtacaaaagt gtgcccaact gtgcaatgaa agtgttcact     780
200  aacgaaggac caacggcttt cttcaagggg ttggtacctt ccttcttgcg acttggatcc     840
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202  cagactatgg actgtgccac ataa                                           924
204 <210> SEQ ID NO: 6
205 <211> LENGTH: 307
206 <212> TYPE: PRT
207 <213> ORGANISM: Homo Sapiens
209 <400> SEQUENCE: 6
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212  Leu Phe Ser Ala Gly Ile Ala Ala Cys Leu Ala Asp Val Ile Thr Phe
213              20                  25                  30
214  Pro Leu Asp Thr Ala Lys Val Arg Leu Gln Val Gln Gly Glu Cys Pro
215          35                  40                  45
216  Thr Ser Ser Val Ile Arg Tyr Lys Gly Val Leu Gly Thr Ile Thr Ala
217      50                  55                  60
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Val Val Lys Thr Glu Gly Arg Met Lys Leu Tyr Ser Gly Leu Pro Ala
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Gly Leu Gln Arg Gln Ile Ser Ser Ala Ser Leu Arg Ile Gly Leu Tyr
                85                  90                  95
Asp Thr Val Gln Glu Phe Leu Thr Ala Gly Lys Glu Thr Ala Pro Ser
            100                 105                 110
Leu Gly Ser Lys Ile Leu Ala Gly Leu Thr Thr Gly Gly Val Ala Val
        115                 120                 125
Phe Ile Gly Gln Pro Thr Glu Val Val Lys Val Arg Leu Gln Ala Gln
    130                 135                 140
Ser His Leu His Gly Ile Lys Pro Arg Tyr Thr Gly Thr Tyr Asn Ala
145                 150                 155                 160
Tyr Arg Ile Ile Ala Thr Thr Glu Gly Leu Thr Gly Leu Trp Lys Gly
                165                 170                 175
Thr Thr Pro Asn Leu Met Arg Ser Val Ile Ile Asn Cys Thr Glu Leu
            180                 185                 190
Val Thr Tyr Asp Leu Met Lys Glu Ala Phe Val Lys Asn Asn Ile Leu
        195                 200                 205
Ala Asp Asp Val Pro Cys His Leu Val Ser Ala Leu Ile Ala Gly Phe
    210                 215                 220
Cys Ala Thr Ala Met Ser Ser Pro Val Asp Val Val Lys Thr Arg Phe
225                 230                 235                 240
Ile Asn Ser Pro Pro Gly Gln Tyr Lys Ser Val Pro Asn Cys Ala Met
                245                 250                 255
Lys Val Phe Thr Asn Glu Gly Pro Thr Ala Phe Phe Lys Gly Leu Val
            260                 265                 270
Pro Ser Phe Leu Arg Leu Gly Ser Trp Asn Val Ile Met Phe Val Cys
        275                 280                 285
Phe Glu Gln Leu Lys Arg Glu Leu Ser Lys Ser Arg Gln Thr Met Asp
    290                 295                 300
Cys Ala Thr
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aggtggtcgg agataccaaa gcaccgtcaa tgcctacaag accattgccc gagaggaagg     600
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L:13 M:270 C: Current Application Number differs, Replaced Current Application No
L:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date

~~23. The method of claim 18, wherein the MHC class II HLA-DR inducing agent~~ is adriamycin.

24. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is gamma interferon.

25. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is selected from the group consisting of a UCR expression vector, a TCRαβ engagement molecule and a fatty acid.

26. The method of claim 18, wherein the endogenous MHC class II HLA-DR ligand is an MHC class II HLA-DR expressing cell.

27. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is administered orally.

~~28. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is administered locally.~~

29. A method for inducing apoptosis in a tumor cell, comprising:

contacting a tumor cell with an amount of a metabolic modifying agent, which when exposed to a cell causes coupling of electron transport and oxidative phosphorylation, effective to increase the mitochondrial membrane potential in the tumor cell, and

contacting the tumor cell with an amount of an apoptotic chemotherapeutic agent effective for inducing apoptosis in the tumor cell.

30. The method of claim 29, wherein the metabolic modifying agent is glucose.

31. The method of claim 29, wherein the metabolic modifying agent is an MHC class II HLA-DP/DQ ligand.

32. The method of claim 29, wherein the metabolic modifying agent is selected from the group consisting of phorbol myristate acetate in combination with ionomycin, GDP, CD40 binding peptide, sodium acetate, UCP antisense, dominant negative UCP,, and staurosporine.

33. The method of claim 29, wherein the metabolic modifying agent is GDP.

34. The method of claim 29, wherein the apoptotic chemotherapeutic agent is selected from the group consisting of adriamycin, cytarabine, doxorubicin, and methotrexate.

35. The method of claim 29, wherein the metabolic modifying agent and the apoptotic chemotherapeutic agent are administered simultaneously.

36. The method of claim 29, wherein the metabolic modifying agent and the apoptotic chemotherapeutic agent are administered locally.

37. The method of claim 35, wherein the tumor cell is resistant to the apoptotic chemotherapeutic agent.

38. The method of claim 29, wherein the tumor cell is sensitive to the apoptotic chemotherapeutic agent, and wherein the amount of metabolic modifying agent is effective to increase mitochondrial membrane potential and the amount of apoptotic chemotherapeutic agent is effective to inhibit the proliferation of the tumor cell when the mitochondrial membrane potential is increased.

~~39. A method for decreasing mitochondrial membrane potential in a cell of a~~ subject, comprising

administering an MHC class II ~~HLA~~-DR ligand to the subject to selectively engage MHC class II HLA-DR on the surface of the cell in an amount effective to decrease ~~mitochondrial membrane potential in the mammalian cell.~~